

INSULIN RECEPTOR ACTIVATORS FOR THE TREATMENT OF  
METABOLIC DISORDERS INDUCED BY TREATMENT WITH HIV  
PROTEASE INHIBITORS

5 CROSS-REFERENCE TO RELATED APPLICATION

This application claims the priority under 35 USC 119(e) of US Provisional  
Application No. 60/239,636, filed October 11, 2000, which is incorporated herein by  
reference.

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BACKGROUND OF THE INVENTION

(a) Field of the Invention

The present invention relates to methods, chemical compounds, and compositions for  
15 the treatment of metabolic disorders induced by treatment with HIV protease inhibitors.

(b) Description of Related Art

Treatments for HIV infection have proven very effective in controlling the ravages of  
the terminal stage of the infection, AIDS. The HIV protease inhibitors are an extremely  
20 important component in the drug regimens used to suppress viral load and the resulting AIDS  
symptoms. Unfortunately, these drugs which are required to maintain health in HIV-infected  
individuals also carry a significant side-effect burden. One of the recently recognized severe  
side-effects is HIV protease inhibitor-induced insulin resistance leading to hyperglycemia that  
can progress to diabetes and ultimately life threatening ketoacidosis. (Carr, A., Samaras, K.,  
25 Chrisholm, D.J., and Cooper, D.A. (1998) *Lancet* 351 1881-1883; Carr, A., Samaras, K.,  
Burton, S., Freund, I., Chisholm, D.J., Cooper D.A. (1998) *AIDS* 12, F51-F58).

In addition to insulin resistance, other related disturbances in metabolism, such as  
lipodystrophy and hypertriglyceridemia, are also observed in HIV protease inhibitor treated  
patients (Roth, V.R., Kravcik, S., Angel, J.B. (1998) *Clin Infect Dis* 27,65-67; Safrin, S., and  
30 Grunfeld, C., (1999) *AIDS* 13, 2493-2505; Carr, A., Samaras, K., Thorisdottir, A., Kaufmann,  
G.R., Chrisholm, D.J., and Cooper, D.A. (1999) *Lancet* 353, 2093-2099; Behrens, G.,